UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,122	08/16/2001	Tony Baker	24219-001CIP2	4239

32301 7590 10/13/2006

CATALYST LAW GROUP, APC
9710 SCRANTON ROAD, SUITE S-170
SAN DIEGO, CA 92121

EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/932,122	BAKER, TONY	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,7,10-19,22,23,26-39,42 and 45-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-7, 10-19, 22-23, 26-39, 42, and 45-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-3, 6-7, 10-19, 22-23, 26-39, 42, and 45-57 are pending and under consideration in the instant application. Claims 4-5, 8-9, 20-21, 24-25, 40-41, and 43-44 were canceled and claims 52-57 were newly added in the amendment filed 7/27/2006. All the amendments and arguments in the response filed 7/27/2006 have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are either newly applied, as necessitated by amendment, or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow, where applicable. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejections made under 35 USC 102, set forth at sections 8 and 10, and the rejection under 35 USC 103, set forth at section 13 of the previous office are withdrawn in view of the amendments to claims 1, 17, and 37 to include concentrations.

4. The rejection under 35 USC 102(b) as anticipated by Sigman, made at section 11 of the previous office action is withdrawn in view of the amendments to include the concentrations in claims 1, 17, and 37 and applicant's arguments that the claimed ranges are less than those recited by Sigman (see page 28, 2nd para of response).

Claim Objections

5. Claim 15 is objected to because of the following informalities: The claim contains a typographical error in the duplicate recitation of "selected from the group" in line 2. Appropriate correction is required. This is maintained and reiterated from the previous office action. No amendment or arguments have been presented concerning this objection.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. Claims 1-3, 6-7, 10-19, 22-23, 26-39, 42, and 45-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to recite concentration ranges such as 'chelator enhancing component(s) is from about 0.1M to about 1.75 M", "about 0.5 M to about 1.50 M" and "0.5 M to about 1.75 M". This amendment has introduced new matter into the claims. The response provides paras 0011 and 0029 (pages 4, and 6-7 of the specification) of the specification for support for the amendments. These paragraphs and the entire specification have been thoroughly reviewed, however the recitation of "1.75M", "about 1.75M", "1.50M", "about 1.50M" "0.5M", and "about 0.5M" are not set forth in the specification. The specification only recites the ranges "about 0.1M to 2M", as well as "at least 1M" for the chelator enhancing components. The specification does not provide support for the specific concept of the newly recited

concentrations. The specification provides no teaching regarding the new specifically recited ranges and limits. For example, MPEP 2163 (I) B states: "New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement."

Claim Rejections - 35 USC § 102

7. Claims 1-3, 6, 10-13, 15-19, 22, 26-29, 31-39, 46-48, 50, 51, and newly added claims 52-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang (WO 95/35390; 12/28/1995) as evidenced by Harvey I (US Patent 6,168, 922) or Harvey II (US Patent 5,939,259) or Collis (Collis et al; US Patent 5,763,185).

The claims are drawn to a method of suppressing the interference of specific masking agents on a molecular assay of a nucleic acid containing test sample (claims 1 and 17) or a method of improving hybridization of nucleic acids by suppressing specific masking agents (claim 37) comprising contacting the test sample with an amount of a divalent metal chelator and a chelator-enhancing component. With regard to claim 37, the recitation of "test nucleic acid" and "target nucleic acid" are interpreted to be any nucleic acid molecule, respectively.

With regard to claims 1-3, 6, 17-19, 22, and 37-39, Zhang teaches a method comprising adding a lysis buffer containing 2.5-5M guanidine thiocyanate and 100mM EDTA and .5% of a detergent to an equal volume of sample (serum) that contains nucleic acids (test nucleic acids) (it is noted that the final concentration of buffer would be 1.25-2.5 M GnSCN and .05M EDTA) (p. 14, lines 8-30) (claims 1, 17, 37, 52-57) and subsequently adding nucleic acid amplification probes (target nucleic acid) and paramagnetic beads to the solution containing lysis buffer and

nucleic acids from the sample. Zhang specifically teaches that hybridization occurs between the nucleic acid from the sample and the probes (p.17, lines 19-20). Zhang specifically teaches that the method can be used for detection of genetic variations in samples from patients with genetic diseases or neoplasia (page 4, lines 13-23, page 5, lines 12-19- eukaryotic DNA).

With regard to claims 31-33, Zhang specifically teaches that samples for the method include whole blood, separated white blood cells, sputum, tissue biopsies, throat swabbings, urine, and serum (see page 13, lines 34-37, page 14, line 11) (claims 31-33).

With regard to the preamble in claims 1, 17, and 37 as well as claims 10-13 and 26-29, although Zhang does not specifically teach inhibition of masking agents set forth in the claim, such is considered a property of the method of Zhang as the addition of the reagents taught by Zhang to the sample taught by Zhang provides for suppression of such masking agents. As evidenced by Harvey ('259), common inhibitors, such as hemoglobin, to nucleic acid amplification can be found in buccal swabs, plasma, serum, sputum, urine and whole blood samples (column 3, lines 55-60). Harvey also teaches that chaotropic salts, such as guanidine thiocyanate (GuSCN) can overcome the problem of hemoglobin inhibition. As evidenced by Collis ('185), nucleic acid hybridization inhibitory substances are derived from heme and hematin which are commonly found in blood samples (col. 1, lines 27-30). Collis teaches that adding chaotropic agents such as guanidine thiocyanate in samples containing inhibitors overcomes this problem (para bridging cols 2-3). With regard to claim 17, which preamble recites "a method of improving the signal response of a molecular assay" and claim 37 which preamble recites "a method of improving hybridization of nucleic acids", such recitations do not distinguish the instantly claimed methods from those of Zhang because Zhang teaches the

positive process steps of the claimed method in the same order, and thus the effects of such necessarily follow. Further, Zhang teaches that wash buffers comprising 1-1.5 M GnSCN and 10 mM EDTA removes unbound proteins that may interfere with subsequent steps (see para bridging pp 17-18).

With regard to claims 36, 48, and 50-51, Zhang teaches molecular assays such as ligation dependent amplification, PCR, and hybridization (abstract, page 33).

Response to Arguments

8. The response traverses the rejection. The response asserts that there is no teaching in Zhang of suppressing interference of a masking agent such as those recited in claim 1. The response asserts that with regard to wash buffers, there is no teaching in Zhang that any of the unbound proteins are any of the masking agents recited in claim 1. The response asserts that with respect to claims 37-41 and 43-47, there is no teaching of improvement in hybridization attributable to the removal of suppression of the specific masking agents recited in the claims. The response further asserts that "there is no actual teaching in Zhang that the use of the actual reagents recited in the claims of the present invention are responsible for the removal of any of the masking agents recited in the claims." These arguments have been thoroughly reviewed but were found unpersuasive as the response argues secondary considerations which cannot overcome a rejection based on 35 USC 102. Zhang teaches addition of reagents set forth in the claims to samples set forth in the claims. The fact that Zhang did not appreciate such secondary considerations does not overcome the fact that Zhang teaches the same steps as those in the instantly claimed methods. The intended use for the methods does not distinguish the claimed

methods over the teaching of Zhang. In the instant case, Zhang teaches the positive process steps of the claimed method in the same order, and the reagents and concentrations used in the method of Zhang are encompassed by instant claims. Further, the claims simply recite adding reagents to a sample containing nucleic acid, which is taught by Zhang in the use of the wash buffer. Therefore, the teachings of Zhang (which include assays which use hybridization and PCR) would necessarily improve hybridization because the reagents and methods of Zhang are the same as those encompassed by the instantly claimed invention. It is noted that claim 37 simply recites that the amounts of divalent metal chelator and chelator enhancing component are selected such that hybridization is improved.

The response asserts that Zhang teaches use of dextran sulfate and a nonionic detergent and that there is no proof in Zhang that any of the masking agents recited in the claims is not due to either or both of these reagents. This argument has been thoroughly reviewed but was found unpersuasive as the claims recite the term "comprising", and do not exclude the use of other reagents. As noted previously, Zhang teaches addition of reagents set forth in the claims to samples set forth in the claims.

The response further asserts that the claims have been amended to recite specific concentrations, which are not taught or suggested by Zhang. This argument has been thoroughly reviewed but was found unpersuasive. The amounts of Zhang's divalent metal chelator and chelator enhancing component, which are present at concentrations ranging from 1.25-2.5 M GnSCN and .05M EDTA are encompassed by the instant pending claims, and therefore Zhang teaches such amounts. Further, Zhang teaches adding 1-1.5M GnSCN and 10 mM EDTA in a wash buffer to a sample containing nucleic acids, as is claimed. Additionally, claim 37 recites

contacting the test solution with target nucleic acid such that hybridization occurs, which is also taught by Zhang. Therefore, Zhang teaches the positive process steps of the claimed method in the same order, and the preamble of the instantly pending claims does not distinguish the instantly pending claims from the teachings of Zhang.

The response asserts that the issue is not "secondary considerations" but that Zhang does not teach that either the guanidine thiocyanate or the EDTA actually removes or suppresses the activity of any masking agents, and that therefore the teachings of Zhang do not necessarily lead to this conclusion. This argument has been thoroughly reviewed but was not found persuasive. The claims simply recite that reagents, which are taught by Zhang, be added to samples to form solutions, which are taught by Zhang. The specification teaches that when the reagents, which are taught by Zhang, are added to samples, such as serum, to form solutions, which is taught by Zhang, the results recited in the claims follow. At page 3, line 21, the specification specifically states: "upon contact with the divalent metal chelators/chelator enhancing components, the masking agents are suppressed." Therefore, the results recited in the preamble do not distinguish from the teachings of Zhang.

Claim Rejections - 35 USC § 103

9. Claims 14, 30, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang, in view of Heath (US Patent 5,973,137).

Zhang teaches a method comprising adding a lysis buffer containing 2.5-5M guanidine thiocyanate and 100mM EDTA and .5% of a detergent to an equal volume of sample (serum) that contains nucleic acids (test nucleic acids) (it is noted that the final concentration of buffer

would be 1.25-2.5 M GnSCN and .05M EDTA) (p. 14, lines 8-30) and subsequently adding nucleic acid amplification probes (target nucleic acid) and paramagnetic beads to the solution containing lysis buffer and nucleic acids from the sample. Zhang specifically teaches that hybridization occurs between the nucleic acid from the sample and the probes (p.17, lines 19-20). Zhang specifically teaches that the method can be used for detection of genetic variations in samples from patients with genetic diseases or neoplasia (page 4, lines 13-23, page 5, lines 12-19- eukaryotic DNA). Zhang specifically teaches that samples for the method include whole blood, separated white blood cells, sputum, tissue biopsies, throat swabbings, urine, and serum (see page 13, lines 34-37, page 14, line 11) (claims 31-33).

Zhang does not teach the addition of an enzyme inactivating component, however Heath teaches that nucleic acid isolation and preservation methods should include anionic detergents, such as SDS or sarkosyl in an amount of .5-3% (col. 6, lines 7-20) for the purpose of lysing cells or solubilizing proteins and lipids as well as denature proteins. Therefor it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Zhang by the addition of SDS or sarkosyl to the composition comprising the EDTA and guanidine. The ordinary artisan would have been motivated to modify the method of Zhang with the addition of SDS or sarkosyl to the composition containing EDTA and guanidine because Heath teaches that such reagents solubilize and denature proteins.

Response to Arguments

10. The response traverses the rejection and asserts that the rejection is specifically traversed because the addition of an enzyme inhibitor as taught by Heath does not remedy the deficiencies

of Zhang. This argument has been thoroughly reviewed but was not found persuasive for the reasons made of record above with regard to Zhang. The response further asserts that there is no incentive provided by the prior art to combine the teachings of Heath and Zhang because Heath is directed to the isolation of RNA at a low ph, which is too low to perform an assay such as PCR. This argument has been thoroughly reviewed but was not found persuasive as the rejected claims do not require PCR. Further, the teachings of Heath were used to set forth that the use of use of the anionic detergents were known in the prior art to be used in lysis reagents for the purpose of solubilizing and denaturing proteins. The rejection did not set forth that the reference of Zhang be used with all of the reagents of Heath.

11. Claims 7, 23, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang, in view of Bertland (Bertland II et al; US Patent 5,030,720).

Zhang teaches the use of a lysis buffer containing a chaotropic agent, stabilizer and detergent in lysing cells in samples such as serum, blood, urine, etc. Zhang specifically teaches a method comprising adding a lysis buffer containing 2.5-5M guanidine thiocyanate and 100mM EDTA and .5% of a detergent to an equal volume of sample (serum) that contains nucleic acids (test nucleic acids) (it is noted that the final concentration of buffer would be 1.25-2.5 M GnSCN and .05M EDTA) (p. 14, lines 8-30) and subsequently adding nucleic acid amplification probes (target nucleic acid) and paramagnetic beads to the solution containing lysis buffer and nucleic acids from the sample. Zhang specifically teaches that hybridization occurs between the nucleic acid from the sample and the probes (p.17, lines 19-20). Zhang specifically teaches that the method can be used for detection of genetic variations in samples from patients with genetic

diseases or neoplasia (page 4, lines 13-23, page 5, lines 12-19- eukaryotic DNA). Zhang does not teach the use of the chaotropic agent, sodium thiocyante or sodium perchlorate, in the lysis buffer. However, sodium thiocyanate and sodium perchlorate were known chaotropic agents at the time the invention was made. For example, Bertland teaches a number of chaotropic agents, such as NaSCN (sodium Thiocyanate) and $NaClO_4$ (sodium perchlorate). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use NaSCN or $NaClO_4$ in the method of Zhang as Zhang teaches to use a chaotropic agent in the lysis buffer and Bertland teaches that NaSCN and $NaClO_4$ are chaotropic agents.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-16 and newly added claims 52 and 53 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,458,546. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are coextensive in scope. The claimed method steps

of the instant application encompass the more narrow methods steps of the claims of the '546 patent. The claims of the '546 patent do not recite a method of suppressing a masking agent, however, the claims are drawn to a method of preserving a nucleic acid in a bodily fluid by adding a reagent containing, for example, EDTA and guanidine thiocyanate to a bodily fluid. Guanidine thiocyanate is a chaotropic agent known to inhibit hybridization inhibitors such as hemoglobin, therefore, suppressing a masking agent is considered a property of the claimed method of the '546 patent. With regard to newly amended claim 1, it is noted that the concentrations claimed overlap in range with those of the claim 1 of the '546 patent and are coextensive in scope.

Response to Arguments

14. The response traverses the rejection. The response asserts that the claims of the '546 application do not recite a method of suppressing a masking agent and that preservation of a sample cannot necessarily be equated with a masking agent. This argument has been thoroughly reviewed but was found unpersuasive as the method steps used in each method are coextensive in scope. The claimed method steps of the instant application encompass the more narrow methods steps of the claims of the '546 patent. The instantly claimed invention encompasses addition of an amount of guanidine, lithium chloride, sodium salicylate, sodium perchlorate or sodium thiocyanate, and an amount of EDTA, EGTA, or BAPTA to a bodily fluid containing nucleic acid. As noted in the instant specification, at page 3, "upon contact with the divalent metal chelator and the chelator enhancing component, the masking agents are suppressed". Claim 1 of the '546 patent is drawn to adding an amount of guanidine, lithium chloride, sodium

salicylate, sodium perchlorate or sodium thiocyanate, and an amount of EDTA, EGTA, or BAPTA to a bodily fluid to. As guanidine isothocyanate is a chaotropic agent which inhibits masking agents forth in the claims, the suppression of a masking agent is considered a property of the claimed method of the '546 patent, as exemplified by the teachings of '546 that the invention "has been found to surprisingly modulate the effect of hemoglobin, e.g., methemoglobin, interference on nucleic acid assays such as PCR..." The arguments specifically made with regard to methmoglobin are not found persuasive as the instant claims are not limited to methemoglobin.

15. Claims 17-48, 50, 51, and newly added claims 54-57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,458,546 in view of Sigman.

Instant claim 17 is drawn to a method of improving the signal response of a molecular assay by interfering with a masking agent by adding a divalent metal chelator and a chelator enhancing component (further drawn to adding such in solution in the range of from about to a test sample, which can be a biological fluid, extracting molecular analytes of interest from the sample, and conducting a molecular assay on the extracted molecular analytes. Instant claim 37 is drawn to a method of improving hybridization by suppressing a masking agent comprising adding a divalent metal chelator and a chelator enhancing component to a test nucleic acid to form a test solution and contacting the test solution with a target such that hybridization occurs. The concentration ranges recited in newly amended claims 17 and 37 overlap with the ranges set forth in claim 1 of '546 and are coextensive in scope.

Claims 1-8 of the '546 patent are drawn to preserving nucleic acids in a biological fluid by contacting the biological fluid with a solution containing a divalent metal chelator in the range of from about 0.001M to about 0.1M and a chelator enhancing component in the range of from about 0.1M to about 2M. Although the claims of the '546 patent do not disclose extracting the nucleic acids and conducting a molecular assay involving hybridization or PCR on the extracted nucleic acids, Sigman teaches a method of isolating and preserving DNA and extracting the isolated and preserved DNA to perform molecular assays, such as hybridization and PCR on the extracted DNA (p. 3, lines 16-19). Sigman specifically teaches that the DNA was extracted (extracting molecular analytes of interest) and electrophoresed (conducting a molecular assay) and T.cruzi nucleic acids were identified. Sigman teaches that there is a need to prepare the DNA for amplification (p. 3, lines 20-21). Sigman specifically teaches a polymerase chain reaction on cleaved minicircle DNA extracted from a blood/GnCl/ EDTA (GEB lysate) sample (see examples 3 and 4). Sigman teaches that using the GEB lysate, PCR amplification of extracted minicircles was sensitive enough that a single T.cruzi cell could be detected in 20 ml of blood (p. 35). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to extract and assay the nucleic acids preserved in the claims of the '546 patent for the purpose of sequencing, or identifying the origin of the DNA preserved, for example to identify infective pathogens in a sample of blood from a patient as taught by Sigman. The ordinary artisan would have been motivated to extract and assay the nucleic acids preserved in the method of the '546 patent for the purpose of identifying such nucleic acids for diagnosing a pathogenic infection, for example. Guanidine thiocyanate is

a chaotropic agent known to reduce the effects of hybridization and PCR inhibitors, therefore, suppressing a masking agent is considered a property of the claimed method of the '546 patent.

Response to Arguments

16. The response traverses the rejection. The response asserts that for the reasons already given, Sigman does not disclose or suggest the suppression by a masking agent or the improvement of a signal response due to the suppression of interference by a masking agent, the combination of Baker and Sigman does not provide basis for the rejection. This argument has been thoroughly reviewed but was not found persuasive for the reasons made of record in the rejection above as well as with regard to the '546 patent in sections 16-17.

Maintained Rejections

Claim Rejections - 35 USC § 103

17. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang, or Sigman, or Harvey I, or Harvey II, (in the alternative), each in view of Ahern (The Scientist; vol. 9, pp 1-5-from the internet; 1995).

Zhang teaches a method comprising adding a lysis buffer containing 2.5-5M guanidine thiocyanate and 100mM EDTA and .5% of a detergent to an equal volume of sample (serum) that contains nucleic acids (test nucleic acids) (it is noted that the final concentration of buffer would be 1.25-2.5 M GnSCN and .05M EDTA) (p. 14, lines 8-30).

Sigman teaches a method of isolating and preserving DNA. Sigman teaches that there is a need to isolate and prevent degradation of DNA in blood samples from patients suspected of

infection with parasites, such as T. Cruzi (eukaryotic DNA) or other infectious agents during storage (p. 3, lines 16-19). Sigman teaches that isolation and storage comprise contacting a biological sample containing DNA in cells with a buffer (aqueous solution) containing a nonamphipathic chaotropic salt (chelator enhancing component) such as guanidine thiocyanate or guanidine chloride and a concentration of a chelating agent. Sigman teaches performing PCR with the preserved nucleic acid.

Harvey I and II teach and claim methods and devices for collecting, storing, and purifying nucleic acids such as DNA or RNA from fluid samples for subsequent genetic characterization by conventional amplification methods (see abstract, claims 1-34). Harvey I and II teach that the device, 903 paper, should be composed of an absorbent material that does not bind nucleic acids irreversibly, impregnated with a chaotropic salt such as guanidine isothiocyanate or sodium perchlorate. Harvey I and II specifically teach a method whereby a square of treated paper (treated with guanidine thiocyanate – see example 1, col. 5) is added to blood which has been collected in a tube containing EDTA (see example 6). Harvey et al teach that DNA was extracted from the paper and subjected to PCR.

Neither Zhang nor Sigman nor Harvey I or II teach the reagents or device in kit format, however Ahern teaches that providing reagents and products in kit format offer scientists the opportunity to better manage their time, and that such kits are convenient. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to package the reagent of Zhang or Sigman, or the device of Harvey I or II in kit format for the purposes of providing premade reagents which are convenient and will save researchers time, as taught by Ahern.

Response to Arguments

18. The response traverses the rejection. The response asserts that since none of the primary references teach suppression of interference by a masking agent in a molecular assay such as PCR, the primary references in combination with Ahern fail to teach or suggest the invention in it's entirety. This argument has been thoroughly reviewed but was found unpersuasive as suppression of a masking agent set forth in the claim is an intended use for the kit and carries no patentable weight. The kit is simply recited to include a reagent which suppresses the interference of a masking agent. The reagents taught by Zhang, Sigman and Harvey, e.g. EDTA, guanidine, are "a reagent for suppressing the interference of a masking agent" including the claimed masking agents as evidenced by the teachings in the specification. Therefore, the properties of the reagents are inherent in references cited. As noted in the MPEP 2111.04 I: "Something which is old does not become patentable upon the discovery of a new property" '[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.' Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999)."

Further, the instructions in the instantly claimed kit are considered printed material and are not given patentable weight. The inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See In re Ngai, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004) (holding that an inventor could not patent known kits by simply attaching a new set of instructions to that product).

Double Patenting

19. Claim 49 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,458,546 in view of Ahern.

Claims 1-8 of the '546 patent are drawn to preserving nucleic acids in a biological fluid by contacting the biological fluid with a solution containing a divalent metal chelator in the range of from about 0.001M to about 0.1M and a chelator enhancing component in the range of from about 0.1M to about 2M. Although the claims of the '546 patent do not disclose the preservative solution in kit format, Ahern teaches that providing reagents and products in kit format offer scientists the opportunity to better manage their time, and that such kits are convenient. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to package the reagent of the '546 patent in kit format for the purposes of providing premade reagents which are convenient and will save researchers time, as taught by Ahern. It is noted that the "use for" the kit carries no patentable weight. Guanidine thiocyanate is a chaotropic agent known to inhibit proteases as well as heme compounds, therefore, suppressing a masking agent is considered a property of the preservative solution recited in the claimed methods of the '546 patent.

Response to Arguments

20. The response traverses the rejection. The response asserts that there is no teaching of the kit of claim 49 when claims 1-8 of the '546 patent and Ahern are combined as the claims 1-8 of '546 patent do not teach or suggest suppression of a masking agent. This argument has been thoroughly reviewed but was found unpersuasive because the use for the kit carries no patentable

weight. The kit is simply recited to include a reagent which suppresses the interference of a masking agent. The reagents taught by '546 claims are reagents which would suppress the interference of a masking agent on a molecular assay. As noted in the instant specification, at page 3, "upon contact of with the divalent metal chelator and the chelator enhancing component, the masking agents are suppressed". The packaging of such kits is obvious over the teachings of claims 1-8 of the '546 patent, in view of Ahern, as set forth above. The instructions in the instantly claimed kit are considered printed material and are not given patentable weight. The inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See In re Ngai, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004) (holding that an inventor could not patent known kits by simply attaching new set of instructions to that product). For these reasons and the reasons already made of record, the rejection is maintained

21. Claim 49 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 19 of copending Application No.11/138,543. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 49 of the instant application is drawn to a kit that comprises a reagent for suppressing the interference of a masking agent on a molecular assay and instructions for use. As defined by the specification such a reagent includes a divalent metal chelator, such as EDTA, EGTA, or BAPTA, and/or a chelator enhancing component, such as lithium chloride, guanidine, sodium thiocyanate, sodium salicylate, and sodium perchlorate. As noted in the instant specification, at page 3, "upon contact of with the divalent metal chelator and the chelator

enhancing component, the masking agents are suppressed". Claim 19 of the '543 application is drawn to a kit comprising a preservative composition comprising an amount of a divalent metal chelator, such as EDTA, EGTA, or BAPTA, in the range of about .001M to 2 M and a chelator enhancing component, such as lithium chloride, guanidinium chloride, guanidinium thiocyanate, sodium thiocyanate, sodium salicylate, and sodium perchlorate, in the range of from about 0.1M to 10 M; a vessel for collecting a fluid; and instructions for use. It is noted that claim 19 of the '543 application is sufficiently broad such that the vessel could contain the preservative composition. The vessel is not recited to contain any specific composition and is not limited to containing a bodily fluid. As such, although instant claim 49 does not recite a container, the reagent would necessarily be contained in a container. Alternatively, the vessel in claim 19 of the '543 application could be a second container. Although the kit in instant claim 49 does not specifically recite a second container, it would have been prima facie obvious to one of ordinary skill in the art to include a container or vessel, in the kit of instant claim 49 so as to provide a container for conducting the molecular assay. The kits are therefore coextensive in scope and not patentably distinct from each other. The use for a kit is given no patentable weight. It is noted that the instructions in each kit are given no patentable weight as they provide an intended use for the claimed kits.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

22. The response traverses the rejection. The response asserts that there is no teaching or suggestion of the suppression of the specific masking agents recited in claim 49. The response asserts that such rejection is analogous to a rejection under 35 USC 103 which means that there is no obviousness type double patenting. This argument has been thoroughly reviewed but was found unpersuasive. Instant claim 49, as exemplified by claims 1-9, 17-25, etc encompass a kit with the same components as that of claim 19 of the '543 application. As noted in the instant specification, at page 3, "upon contact of with the divalent metal chelator and the chelator enhancing component, the masking agents are suppressed" (such divalent metal chelator and chelator enhancing components of the claimed kit of the '543 application). With regard to the analogy to a rejection under 35 USC 103, it is noted that the MPEP, section 2144 "Rationale different from applicant's is permissible" states that rationale can be different from applicant's:

> The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991) (discussed below). Although Ex parte Levengood, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done" (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention.

Accordingly, as the kit in the instant application and the kit of the '543 application are coextensive in scope, and the instructions for each kit is given no patentable weight and does not distinguish the kits, the rejection is maintained.

23. Claim 49 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12, 13, 17, and 18 of copending

Application No. 11/138,543 in view of Ahern. Claim 49 of the instant application is drawn to a kit that comprises a reagent for suppressing the interference of a masking agent on a molecular assay and instructions for use. As defined by the specification such a reagent includes a divalent metal chelator, such as EDTA, EGTA, or BAPTA and/or a chelator enhancing component, such as lithium chloride, guanidine, sodium thiocyanate, sodium salicylate, and sodium perchlorate. Such a reagent can also include an enzyme inactivating component, such as manganese chloride, sarkosyl, and SDS. Claims 12 and 18 of the '543 application are drawn to a preservative composition comprising an amount of a divalent metal chelator, such as EDTA, EGTA, or BAPTA, in the range of about .001M to 2 M, or more specifically at least .01M; and a chelator enhancing component, such as lithium chloride, guanidinium chloride, guanidinium thiocyanate, sodium thiocyanate, sodium salicylate, and sodium perchlorate, in the range of from about 0.1M to 10 M, more specifically at least 1 M. Claims 13 and 17 are further drawn the composition containing an enzyme inactivating component, such as manganese chloride, sarkosyl, and SDS, in the range of up to 5% molar concentration. As such, the reagent in the kit of instant claim 49 and the composition of claims 12, 13, 17, 18 of the '543 application are coextensive in scope. Claims 12, 13, 17, and 18 of the '543 application do not recite packaging the composition in kit format, however Ahern teaches that providing reagents and products in kit format offers scientists the opportunity to better manage their time, and that such kits are convenient. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to package the reagent composition of the '543 application in kit format for the purposes of providing premade reagents which are convenient and will save researchers time, as taught by Ahern. It is noted that the "use for" the kit carries no patentable weight.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

24. The response traverses the rejection. The response asserts that there is no teaching or suggestion of the suppression of the specific masking agents recited in claim 49 in the claims of the '543 application. The response further asserts that Ahern doe not provide the information necessary to create the obviousness type double patenting rejection, which is considered to be analogous to a rejection under 35 USC 103. These arguments have been thoroughly reviewed but were found unpersuasive for the reasons already made of record above.

Conclusion

25. No claims are allowable over the cited prior art.

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton
Primary Examiner
Art Unit 1634
10/5/06